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## CASE REPORT

# Successful treatment of chronic hepatitis B and D with pegylated-interferon plus entecavir

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hepatitis B surface antigen;  
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combination therapy

Interferon-based regimen has been used to treat hepatitis D virus (HDV) super-infection on top of hepatitis B virus (HBV) carriers; however, viral relapse is frequent after stopping therapy. Recently, quantitative hepatitis B surface antigen (qHBsAg) was introduced to help the management of chronic hepatitis B (CHB). Little is known about its role in the treatment of HBV and HDV dual infection. Herein, we reported a 45-year-old male HBV carrier with HDV co-infection who received combination therapy of pegylated-interferon  $\alpha$ -2a plus entecavir. The qHBsAg level was adopted as the treatment guidance and a consolidation therapy of 12 months was continued after HBsAg loss. The patient achieved HBsAg seroconversion with HDV RNA undetectable after 35 months of combination therapy and sustained therapeutic response 12 months post-therapy. Therefore, personalized response-guided therapy by using qHBsAg may be an option for the treatment for HBV and HDV dual infection.

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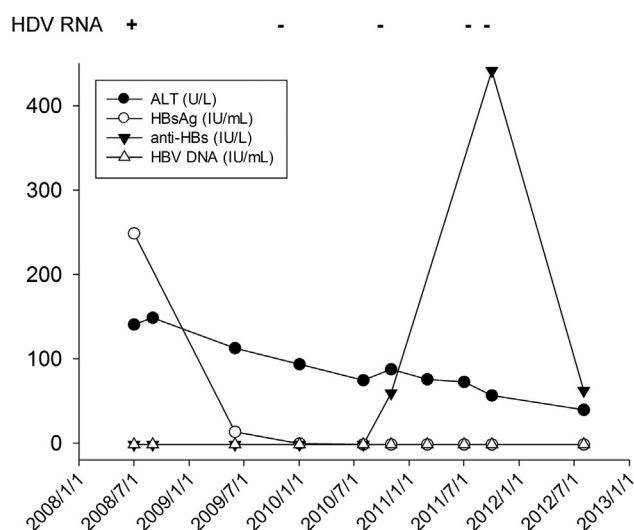
An interferon-based regimen has been used to treat hepatitis D virus (HDV) superinfection on top of HBV carriers; however, viral relapse occurs frequently after stopping

therapy. Recently, quantitative hepatitis B surface antigen (qHBsAg) was introduced to help with the management of chronic hepatitis B.<sup>1,2</sup> Little is known about its role in the

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**Figure 1** The treatment responses of dual HBV-HDV infection in this patient.

treatment of HBV and HDV dual infection. Herein, we report an HBV carrier with HDV dual infection, who received combination therapy of pegylated-interferon  $\alpha$ -2a plus entecavir. The qHBsAg level was adopted as the treatment guidance with a good sustained response.

A 45-year-old Taiwanese man with HBeAg-negative genotype C chronic hepatitis B, had a persistent elevation of serum alanine aminotransferase (ALT), despite effective treatment with oral entecavir (0.5 mg) for 13 months (with undetectable HBV-DNA level for 10 months). At his first visit, laboratory data showed ALT elevation (142 U/L, normal limit: <41 U/L), positive HBsAg (>250 IU/mL), negative anti-HCV, and HBV-DNA level <10 IU/mL. Other etiologies of hepatitis including alcoholic, autoimmune, cholestatic, hereditary, drug and steatohepatitis were excluded by clinical and laboratory evidence. The liver histology revealed advanced fibrosis (Metavir score: F3) with active inflammation (Histology-Activity-Index score: 10). Serum qualitative HDV-RNA was positive by the polymerase chain reaction (PCR). With the diagnosis of HBV and HDV dual infection, the patient received combination therapy of weekly pegylated-interferon  $\alpha$ -2a 180  $\mu$ g, plus daily entecavir (0.5 mg) since September 2008. Declines of ALT and qHBsAg levels were noted and followed by HBsAg loss at 23 months of combination therapy. In addition, serum HDV-RNA became undetectable after 13 months of therapy. Moreover, improvement of hepatic fibrosis was documented by Fibroscan

(5.7 kPa, corresponding to Metavir score: F0–F1). A consolidation therapy after HBsAg loss was administered for 1 more year. HBsAg seroconversion, with a protective level of anti-HBs and ALT normalization, was achieved at 25 months of treatment. Thus, a sustained treatment response was noted for more than 12 months after stopping combination therapy (Fig. 1).

Conventional or pegylated-interferon- $\alpha$  is the only agent for the treatment of HBV and HDV dual infection; however, the sustained HDV clearance rate was only 25–30% after 1 year of treatment with a high viral relapse.<sup>3</sup> The addition of oral ribavirin, adefovir, or lamivudine to interferon did not show additional benefits.<sup>4</sup> The efficacy of entecavir monotherapy for HDV infection was poor, probably because of short treatment duration and no HBsAg decline during therapy.<sup>5</sup> The major challenge for the treatment of HBV and HDV dual infection is the higher rate of viral relapse after discontinuation of therapy. Theoretically, the best therapeutic endpoint of HBV and HDV dual infection is HBsAg seroclearance. If serum HBsAg remains detectable in treated patients, the residual intrahepatic HDV may reactivate into a full blown infection and recapitulate hepatitis D.<sup>3</sup>

In this case report, the combination of pegylated interferon  $\alpha$ -2a plus entecavir might be effective for the treatment of HBV and HDV dual infection. In addition, serum qHBsAg level may be a good guidance for treatment duration and 1 year consolidation therapy post HBsAg seroconversion could be considered to increase the sustained response rate.

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